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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,605	08/14/2007	Haruo Sugiyama	14875-170US1 C1-A0403P-US	4985
26161 7590 10/14/2011 FISH & RICHARDSON P.C. (BO) P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER BELYAVSKYI, MICHAIL A	
			ART UNIT 1644	PAPER NUMBER
			NOTIFICATION DATE 10/14/2011	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No. 10/594,605	Applicant(s) SUGIYAMA ET AL.	
	Examiner MICHAEL BELYAVSKYI	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 1-4, 7 and 9-17 is/are pending in the application.
- 5a) Of the above claim(s) 2 and 7 is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 1, 3-4 and 9-17 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

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RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/23/11 has been hereby entered.

Claims 1-4, 7 and 9-17 are pending.

3

Claims 2 and 7 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1, 3-4 and 9-17 read on the method of separating hepatic, endothelial or hematopoietic progenitor cells from cell population, comprising detecting the expression of WT1 gene are under consideration in the instant application.

In view of the amendment, filed 09/23/11 the following rejections remain

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1,3-4 and 9-17 stand rejected under 35 U.S.C. 103(a) as being unpatentable over EP0846949 (IDS) in view of Fraizer et al (Blood, 1995, v.86, pages 4704-4706) and WO' 97/39354 (IDS) or Menssen et al (Blood, 1997, v.89, pages 3486-3493, IDS) , or Baird et al (Exp Hematol, 1997, v.13, pages 1311-1312, IDS) or Loeb et al., (Leukemia, 2003, v.17, pages 965-971) or Tsubio et al (Leukemia Research, 1999, v.23, pages 499-505) for the same reasons set forth in the previous Office Action, mailed on 08/30/10.

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Applicant's arguments filed on 09/23/11 have been fully considered but have not been found convincing.

Applicant asserts that: (i) EP '949 does not disclosed or suggested the use of WT1 expression as a marker for hepatic, endothelial or hematopoietic progenitor cells or specific expression ranges recited in the amended claims; (ii) the levels of expression of WT1 in hematopoietic cells disclosed in Fraizer et al., (Table 1) is higher than that recited in the claims; (iii) Menssen et al., do not teach or suggest the use of a reporter gene or detection of WT1 expression in a viable cells; (iv) none of the prior art references recited by the Examiner teaches or suggest the use of detection of WT1 expression in a viable cells.

Contrary to Applicant's assertion, it has been recently stated that KSR forecloses the argument that a specific teaching, suggestion, or motivation are required to support a finding of obviousness See Board decision (see *KSR International Co v Teleflex Inc.*, 550U.S.-, 82 USPQ2d 1385, 2007).

Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see *In re Keller*, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. *In re Young* 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

EP 949 teaches a method of detecting and separating a specific cells from the cell population based on the level of expression of WT1 gene (see entire document, Abstract and pages 3, and 5 in particular). EP 949 teaches that said cells can be CD34- cells or solid cancer cells (see page 5 and 6 in particular).

EP 949 does not explicitly teaches a method for separation hepatic, endothelial or hematopoietic progenitor cells from the cell population, based on the specific levels of expression of WT1 gene.

Fraizer et al., teach the high level of expression of WT-1 gene in a population of hematopoietic progenitor cell (see entire document, Abstract in particular). Fraizer et al., teach that expression of WT1 may be used as a clinical marker for immature MB cells expressing a high level of WT1 (see page 4705 in particular).

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With regards to Applicant's comments that the levels of expression of WT1 in hematopoietic cells disclosed in Fraizer et al., (Table 1) is higher than that recited in the claims.

It is noted that in Table 1, Fraizer et al., disclosed quantitated WT1 mRNA levels relative to b actine mRNA for various cells without normalization for K562 leukemia cells . Moreover, it is noted that said reference was used to show that at the time the invention was made one skilled in the art would know that expression of WT1 may be used as a clinical marker for progenitor cells. Though Fraizer et al., do not explicitly teach the expression ranges, as recited in the instant claims, it would be conventional and within the skill of the art to identify and determine the optimum expression ranges. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also *Merck & Co. v. Biocraft Labs. Inc.*, 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

WO'354 teaches the high level of expression of WT-1 gene in a population of hematopoietic progenitor cell (see entire document, Abstract in particular).

Menssen et al ., teach the high level of expression of WT-1 gene in a population of hematopoietic progenitor cell (see entire document, page 3486 in particular). Menssen et al., teach that expression of WT1 may be used as a clinical marker for immature CD34+ cells expressing a high level of WT1 (see page 3487 in particular).

Baird et al., ., teach the high level of expression of WT-1 gene in a population of hematopoietic progenitor cell (see entire document, Abstract in particular). Baird et al., teach that expression of WT1 gene was detected by using expression of WT1 gene.

Loeb et al ., teach the high level of expression of WT-1 gene in a population of hematopoietic progenitor cell (see entire document, abstract and page 969 in particular). Loeb et al., teach that expression of WT1 gene was detected by using expression of WT1 gene.

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Tsuboi et al., teach the high level of expression of WT-1 gene in a population of hematopoietic progenitor cell (see entire document, page 499 in particular). Tsuboi et al., teach that expression of WT1 may be used as a clinical marker for immature CD34+ cells expressing a high level of WT1 (see page 504 in particular). Tsuboi et al., teach that expression of WT1 gene was detected by using expression of WT1 gene.

With regards to Applicant's comments that none of the prior art references recited by the Examiner teaches or suggest the use of detection of WT1 expression in a viable cells.

The Examiner strongly disagrees with said statement.

In particular, Menssen et al., teaches " we report on WT1 gene expression in umbilical cord blood cells of human fetuses aged between 19 and 34 weeks of gestation. We found WT1 gene expression in normal hematopoietic progenitors only during the early exponential growth phase when propagated in clonal growth assays". (see page 3486 in particular). It is Examiner position that it would be immediately obvious to one skill in the art that Menssen et al., refers to viable cells.

Similarly, Tsuboi et al., teach that " we describe here that constitutive expression of WT1 gene in hematopoietic progenitor cells promotes their proliferation" (see page 500 in particular). It is Examiner position that it would be immediately obvious to one skill in the art that Tsuboi et al., refers to viable cells.

All the claimed elements were known in the prior art and one skill in the art could have combine the elements as claimed by known methods with no change in their respective function and the combination would have yield predictable results to one of ordinary skill in the art at the time of the invention (see *KSR International Co v Teleflex Inc.*, 550U.S.-, 82 USPQ2d 1385, 2007).

Thus it would have been obvious to one of the ordinary skill in the art at the time the invention was made to use expression of WT1 gene as a marker for separation hematopoietic progenitor cells from the cell population with a reasonable expectation of success because the prior art suggests that high level of expression of WT-1 gene in a population of hematopoietic progenitor cell and thus can be used as a marker to separate the cells expressing WT1 gene by the method taught in the prior art of EP'949.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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8. No claim is allowed.

9. This is an RCE of applicant's earlier Application No. 10/594,605. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. **THIS ACTION IS MADE FINAL.** See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571/ 272-0735

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michail A Belyavskiy/
Primary Examiner, Art Unit 1644

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